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Modern Concepts of Cardiovascular Disease

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ERYTHEMATOUS LUPUS (LUPUS ERYTHEMATOSUS)

Nomenclature. Erythematous Lupus has been known to dermatologists for more than 80 years under the more imposing title, Lupus Erythematosus Disseminatus seu Erythematodes. Its dermatologic designation as Lupus has served to confuse it with such totally different conditions as Lupus Vulgaris, a tuberculous affection of the skin, and with Discoid Lupus, a localized but harmless skin lesion of the face of unknown cause. Erythematous Lupus is not a primary disease of the skin. It is a dramatic and usually fatal disease of the body as a whole.

Sex and Age. The disease may be observed in children as young as 6 or 8 years and in women up to the menopause. Unlike rheumatic fever and rheumatoid arthritis, erythematous lupus is predominantly a disease of females. Although it may occur in adolescent boys and in young men, they constitute less than 5 percent of the cases in an unselected series. Some examples of the disease have been observed among the young men in our armed forces, but they have been extremely rare. The fact that more than 95 percent of the cases occurring in the general population are females has led clinicians to search for an endocrine disorder, but no abnormalities in the glands of internal secretion have been found; nor have the rare male cases shown any endocrinologic peculiarities.

Etiology. The predominant predilection of females can merely be interpreted as meaning that the constitutional factor of sex is a strong predisposing influence. This overwhelming influence of sex is comparable to the converse predilection of males for thromboangiitis obliterans, and is equally inexplicable.

The cause of the disease remains as obscure as that of rheumatic fever and of rheumatoid arthritis.

Pathology. The disease seems to exhibit its effect primarily upon the collagenous tissue of the body which serves as a matrix or binding substance for capillaries and arterioles throughout the body.

The effect of this collagen change is reflected most conspicuously in the smaller blood vessels of the viscera (kidneys, heart, lungs, liver, pancreas, spleen, skin, ovaries, etc.) Wherever it occurs in the walls of vessels, it results in proliferative lesions of the lining endothelium and in degenerative and necrotic lesions of blood vessel walls associated with thrombi which often occlude the lumen. In affected glomeruli the changes may consist of proliferative, thrombotic or necrotic lesions of glomerular loops. In about half the cases, the glomeruli present a peculiar hyaline swelling of the collagen fibrils in the capillary walls. The latter may result in a characteristic thickening and stiffening of the capillary walls so that the glomerular loops look rigid and thick as if made of heavy bent wire, a picture which has been described as the "wire loop lesion."

Pleural, pericardial and even peritoneal adhesions and seroplastic exudates are commonly encountered, the evidences of attacks and serositis. Effusions may occasionally be found in any of the serous cavities. Bronchopneumonia or other secondary infections are common terminal complications.

In 20 to 25 percent of all the cases which come to necropsy, proliferative and thrombotic lesions occur on the valves or walls of the heart. The lesion begins as a degeneration of the subendothelial collagenous tissue which swells so as to form an excrescence on the surface of the endocardium. Libman and Sacks, who first called attention to this lesion, designated it as indeterminate endocarditis to distinguish it from endocardial vegetations due to known bacteria. This is to be found only in the severest cases. The vegetations may be small and verrucous or broad and flat. They may occur on both sides of the valve cusps, extend down the chordae tendineae and may involve even the mural endocardium.

In another 20 percent a row of coarse verrucae may occur on the mitral or tricuspid valves which resemble the so-called "terminal endocarditis" seen in persons dying after carcinoma and other prolonged wasting diseases. Aschoff bodies are not found in the myocardium.

In at least half the cases of erythematous lupus, the endocardium appears to be entirely normal.

The skin may show collagen changes amounting in places to fibrinoid degeneration. The smaller vessels may be involved as in the kidneys and other viscera. ing in places to fibrinoid degeneration. The smaller vessels may be involved as in the kidneys and other viscera.

Clinical Picture. The onset is usually insidious, with weakness, fatigue and fever. When arthralgias occur at this stage the clinical picture may be indistinguishable from rheumatic fever. The febrile course continues with irregular periods of exacerbation during which the temperature may be as high as 105°. The blood count may give the first diagnostic clue, for a leukopenia (3500 to 6000 leucocytes) is regularly present. When secondary infections of the skin or resipratory tract occur as intercurrent complications, leukopenia may be replaced temporarily by leucocytosis and polynucleosis.

As the disease continues, the hemoglobin and red cell count fall to moderately low levels (60 to 75 percent) and the blood platelets are reduced to 75,000 to 150,000, rarely as low as 40,000. The leukopenia, thrombopenia and hypochromic anaemia appear to be due to a depression of hematopoiesis. The Wassermann test is usually negative but may temporarily become positive or anticomplementary.

The finding of leukopenia in a case of prolonged fever and arthralgia should encourage a careful examination of the urine for red blood cells which may be the first indication of vascular lesions in the kidneys. The presence of microscopic hematuria and albuminuria may at first give rise to a suspician of glomerulonephritis. Later in the disease the progressive injury to the vascular system of the kidneys may finally induce sufficient damage to renal parenchyma to cause a fixation of the specific gravity and, in the last weeks of the disease, azotemia. In spite of the systemic and renal vascular injury, the blood pressure is usually normal, occasionally moderately elevated.

The rash may be present during the first weeks of the illness or its appearance may be delayed for months until the terminal period of the disease. In exceptional instances it may be absent throughout the entire clinical course. Sometimes its first appear-

ance may follow excessive exposure to sunlight or to wind and may coincide with the onset of a severe exacerbation of the disease. In its absence the clinical picture of extreme weakness, prolonged fever and arthritis, sometimes an attack of pericarditis or pleuritis, has led to an erroneous diagnosis of rheumatic fever and, during a temporary remission in the disease, convalescence in a warm climate with much sunlight has, therefore, been prescribed, only to be followed by the appearance of a full blown eruption and an intensification of the disease process. In many cases no exposure to sunlight precedes the onset of the rash. In fact, sunlight would appear to be only one form of truama which can increase the vascular damage in skin in which the vessels are already diseased. The erythema is characteristically located on the bridge of the nose and extends in a butterfly pattern over the cheeks and the malar eminences. At first it may be macular or blotchy but soon becomes confluent. As it extends, other prominent portions of face may become involved, the superciliary ridges, the chin, upper lip, edges of the pinna. The V-shaped exposed area over the manubrium is commonly involved. The shaded areas of the face and neck usually remain uninvolved. Although sunlight and wind may bring on or intensify the rash of these exposed parts, the mere truama of rubbing against the bed clothes may induce erythematous patches in the skin over the shoulders, elbows, knees and malleoli.

At times the erythema has a slight bluish cast. Often punctuate hemorrhages and telangiectases are to be seen in the erythematous patches. These are minute petechiae or else dilated capillaries or arterioles surrounded by exuded serum and red cells which have permeated through the diseased vessel walls into the corium. Petechiae are more common when the blood platelet count is unusually low. After the disease has lasted many months, a moderate edema of the face and extremities may occur in patients in whom the vascular injury has been unusually severe and there has been persistent albuminuria. Blood examinations usually reveal hypoproteinaemia. In a third of the cases the hands and feet are involved and in rare instances the rash may even be limited to the extremities. Small patches of erythema may be located on the palmar (and plantar) surface of the terminal phalanges and on the skin around the nail beds; also erythematous macules may be visible on the thenar and hypothenar eminences of the palms and on the ball and heel of the feet. In the midst of the erythema there are sometimes petechial hemorrhages and telangiectases. In rare cases with the most intense skin lesions, hemorrhagic blebs may appear on the erythematous areas of the fingers, toes and pinna due to exudation of serum and red cells from the diseased vessels in the skin. At the height of the disease erythematous or petechial macules may appear on the mucous membranes, especially of the mouth, which sometimes break down to form small shallow ulcers surrounded by an erythematous or hemorrhagic areola. These lesions tend to heal.

Effusions which are usually the result of a serositis may occur into the pleura and, rarely, the pericardium. More commonly a dry pleurisy or pericarditis with chest pain and friction rub precedes the development of the serous effusion. Pleuritis and pericarditis may occur at any time during the disease; attacks are almost as common and as characteristic as in rheumatic fever. In some cases the serositis may involve the peritoneum and give rise to abdominal pain, tenderness and rigidity. Patients have been operated upon needlessly because of an erroneous diagnosis of some other intra-abdominal inflammatory disease.

When the rash is extensive, discrete lymph nodes may be palpable in the cervical, axillary and inguinal regions. The spleen is palpable only in a minority of the cases, and then usually because of an intercurrent infection.

In advanced cases the ophthalmoscopic lesions are characteristic. They consist of perivascular hemorrhages and fluffy exudates adjacent to obviously diseased arterioles showing segmentation. Circumpapillary oedema may be present and even flame shaped hemorrhages. The retinal changes are due entirely to the local vascular disease for they occur in cases in which the blood pressure has been consistently normal, in striking contrast to the fundus lesions of so-called malignant hypertension.

The heart presents no characteristic clinical findings. Systolic murmurs at the apex, when present, are difficult to interpret, for they may be due to anaemia, fever, and a toxic effect upon the myocardium. It is rarely possible to ascribe them positively to an endocardial valvular lesion. When the fever is high and the patient is extremely toxic, gallop rhythm is apt to occur. The electrocardiogram reveals either no abnormalities or else low voltage as evidence of the toxic damage to the myocardium.

Death usually follows after an illness of three to six or more months. In some instances partial or complete remissions may last for months or even several years during which the temperature may be normal and yet the arthritis and rash may recur from time to time. In a few instances complete recovery has occurred. In most cases, however, death supervenes after a more or less prolonged febrile course, due to the toxemia of the disease, to renal insufficiency (azotemia) or to an intercurrent infection of the respiratory tract.

Therapy. In the absence of knowledge concerning the cause of the disease, its treatment is as yet largely symptomatic and empirical. High fever and arthralgia may usually be ameliorated with salicylates as in rheumatic fever and the drug may also have a favorable effect upon the resorption of serous effusions. When the latter occur in the late stages of the disease in association with more general edema due to hypoproteinaemia and anaemia, transfusions with whole blood or plasma are indicated. They must be given by slow drip, not more than 60 drops a minute and not more than 500 cc a day if there is a tendency to gallop rhythm or other evidences of impending heart failure.

Although the patients are not photosensitive in the true sense as in hydroa aestivale and porphyrinaemia, intensification of the erythema is easily induced even by slight exposure to sunlight and this may coincide with an increase in the general severity of the disease. It is, therefore, advisable to protect them by darkening the room with drawn window shades or by pasting red cellophane on the window panes.

During the febrile periods, small doses of sulfadiazene (1.0 gram twice a day) may help in preventing secondary infections of the respiratory tract and other parts of the body. The tendency to leukopenia characteristic of the disease does not contraindicate its use, but blood counts should be done twice a week. In the presence of an intercurrent bacterial infection, large doses of an appropriate sulfonamide or of penicillin are indicated. Neither sulfonamides nor penicillin influence the primary disease process.

Because of the female predilection, testosterone and stilbestrol have been employed but without any significant effect upon the clinical course. Ovariectomy and artificial menopause by roentgentherapy have been recommended but there is no evidence that they are curative.

The diet should not be restricted and should be well balanced. It is especially important to maintain an adequate protein intake. An adequate intake of large doses of all the elements in the B complex is important for there is usually a deficiency to be corrected as in any prolonged febrile illness. Because of the low blood levels of vitamin C, saturation with civatamic acid and an adequate intake of fresh citrus fruits are indicated. But no influence on the primary disease process has been noted.

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